

=> d his

(FILE 'HOME' ENTERED AT 14:59:11 ON 22 AUG 2006)

FILE 'REGISTRY' ENTERED AT 14:59:37 ON 22 AUG 2006

EXP TIOTROPIUM/CN  
L1 10 S E3-E12  
EXP OXATROPIUM/CN  
EXP OXITROPIUM/CN  
L2 2 S E3-E4  
EXP IPRATROPIUM/CN  
L3 2 S E3-E4  
L4 0 S CLIOMILAST/CN  
EXP ARIFLO/CN  
L5 1 S ARIFLO/CN  
L6 1 S ENPROFYLLINE/CN  
L7 1 S ROFLUMILAST/CN  
L8 STRUCTURE uploaded  
L9 0 S L8  
L10 23 S L8 SSS FULL

FILE 'CAPLUS' ENTERED AT 15:04:11 ON 22 AUG 2006

881 S L1 OR L2 OR L3  
556 S L5 OR L6 OR L7 OR L10  
L13 26 S L11 AND L12  
L14 10 S L13 AND (ASTHSMA OR COPD OR (CHRONIC(W) OBSTRUCTIVE(W) PULMONAR  
L15 0 S L14 NOT PY>2001  
L16 0 S L14 NOT PY>2002  
L17 237 S L11 AND (ASTHSMA OR COPD OR (CHRONIC(W) OBSTRUCTIVE(W) PULMONAR  
L18 51 S L17 NOT PY>2001  
L19 11 S L18 AND TIOTROPIUM  
L20 0 S L19 AND ASTHSMA  
L21 3 S L19 AND ASTHMA  
L22 0 S L12 AND ASTHSMA AND (COPD OR (CHRONIC(W) OBSTRUCTIVE(W) PULMONA  
L23 85 S L12 AND (COPD OR (CHRONIC(W) OBSTRUCTIVE(W) PULMONARY(W) DISEASE  
L24 14 S L23 NOT PY>2001

=>

=> d his

(FILE 'HOME' ENTERED AT 16:24:23 ON 22 AUG 2006)

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE, AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS, CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 16:24:33 ON 22 AUG 2006  
SEA (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4)

-----  
1 FILE BIOSIS  
6 FILE CAPLUS  
1 FILE DRUGU  
52 FILE IFIPAT  
2 FILE PHIN  
2 FILE PROMT  
6 FILE PROUSDDR  
1 FILE RDISCLOSURE  
1 FILE SCISEARCH  
1 FILE TOXCENTER  
201 FILE USPATFULL  
27 FILE USPAT2  
32 FILE WPIDS  
6 FILE WPIFV  
32 FILE WPINDEX  
1 FILE DPCI  
36 FILE EPFULL  
16 FILE INPADOC  
305 FILE PCTFULL

L1 QUE (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4)

-----  
FILE 'USPATFULL, EPFULL, PCTFULL' ENTERED AT 16:26:03 ON 22 AUG 2006

L2 542 S (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4)  
L3 514 S (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4 (W) INHIBIT?)  
L4 6 S L3 NOT PY>2001

=>

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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Property values tagged with IC are from the ZIC/VINITI data file  
provided by InfoChem.

STRUCTURE FILE UPDATES: 21 AUG 2006 HIGHEST RN 903048-34-0  
DICTIONARY FILE UPDATES: 21 AUG 2006 HIGHEST RN 903048-34-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and  
predicted properties as well as tags indicating availability of  
experimental property data in the original document. For information  
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

```
=> exp tiotropium/cn
E1      1    TIOTRIAZAZIN/CN
E2      1    TIOTRIFAR/CN
E3      1 --> TIOTROPIUM/CN
E4      1    TIOTROPIUM BROMIDE/CN
E5      1    TIOTROPIUM BROMIDE MONOHYDRATE/CN
E6      1    TIOTROPIUM CHLORIDE/CN
E7      1    TIOTROPIUM HYDROGEN PHOSPHATE/CN
E8      1    TIOTROPIUM IODIDE/CN
E9      1    TIOTROPIUM METHANESULFONATE/CN
E10     1    TIOTROPIUM METHYLSULFATE/CN
E11     1    TIOTROPIUM P-TOLUENESULFONATE/CN
E12     1    TIOTROPIUM PHOSPHATE/CN

=> s E3-E12
1 TIOTROPIUM/CN
1 "TIOTROPIUM BROMIDE"/CN
1 "TIOTROPIUM BROMIDE MONOHYDRATE"/CN
1 "TIOTROPIUM CHLORIDE"/CN
1 "TIOTROPIUM HYDROGEN PHOSPHATE"/CN
1 "TIOTROPIUM IODIDE"/CN
1 "TIOTROPIUM METHANESULFONATE"/CN
1 "TIOTROPIUM METHYLSULFATE"/CN
1 "TIOTROPIUM P-TOLUENESULFONATE"/CN
1 "TIOTROPIUM PHOSPHATE"/CN
L1      10 (TIOTROPIUM/CN OR "TIOTROPIUM BROMIDE"/CN OR "TIOTROPIUM BROMIDE
          MONOHYDRATE"/CN OR "TIOTROPIUM CHLORIDE"/CN OR "TIOTROPIUM
          HYDROGEN PHOSPHATE"/CN OR "TIOTROPIUM IODIDE"/CN OR "TIOTROPIUM
          METHANESULFONATE"/CN OR "TIOTROPIUM METHYLSULFATE"/CN OR "TIOTROPIUM
          P-TOLUENESULFONATE"/CN OR "TIOTROPIUM PHOSPHATE"/CN)
```

=> d 11

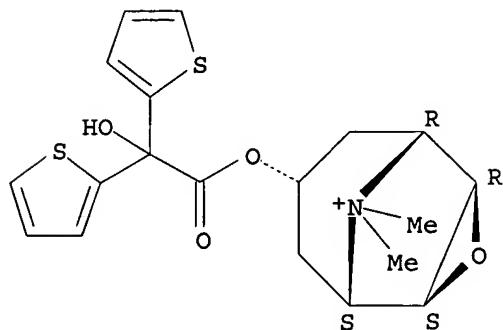
```
L1      ANSWER 1 OF 10  REGISTRY  COPYRIGHT 2006 ACS on STN
RN      851029-97-5  REGISTRY
ED      Entered STN: 24 May 2005
CN      3-Oxa-9-azoniabicyclo[3.3.1.02,4]nonane, 7-[(hydroxydi-2-
          thienylacetyl)oxy]-9,9-dimethyl-, (1 $\alpha$ ,2 $\beta$ ,4 $\beta$ ,5 $\alpha$ ,7 $\beta$ -
          a.)-, phosphate (2:1) (salt) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN      Tiotropium hydrogen phosphate
FS      STEREOSEARCH
```

MF C19 H22 N O4 S2 . 1/2 H O4 P  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

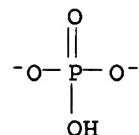
CRN 186691-13-4  
CMF C19 H22 N O4 S2

Relative stereochemistry.



CM 2

CRN 14066-19-4  
CMF H O4 P



1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> exp oxatropium/cn

E1	1	OXATRISTANNETANE/CN
E2	1	OXATRISTANNETANE, HEXAKIS(2,6-DIETHYLPHENYL)-/CN
E3	0	--> OXATROPIUM/CN
E4	1	OXAUNOMYCIN/CN
E5	1	OXAWAX TS 254A/CN
E6	1	OXAWAX TS 254AA/CN
E7	1	OXAYOHIMBAN/CN
E8	1	OXAYOHIMBAN, B-D-GLUCOPYRANOSIDE DERIV./CN
E9	1	OXAYOHIMBAN, 1-PROPANAMINIUM DERIV./CN
E10	1	OXAYOHIMBAN, 16,17-DIDEHYDRO-19-METHYL-, (19A,20.ALPHA.)-(-)-/CN
E11	1	OXAYOHIMBAN, 16,17-DIDEHYDRO-19-METHYL-, (3B,19B)-(-)-/CN
E12	1	OXAYOHIMBAN, 17-METHOXY-19-METHYL-, (17A,19B)-/CN

=> exp oxitropium/cn

E1	1	OXITRIPTAN/CN
E2	1	OXITRIPTYLINE/CN
E3	1	--> OXITROPIUM/CN
E4	1	OXITROPIUM BROMIDE/CN
E5	1	OXIURAN/CN

```

E6      1      OXIVENT/CN
E7      1      OXIVOR/CN
E8      1      OXIYANT/CN
E9      1      OXIZINOVOR/CN
E10     1      OXKI 1/CN
E11     1      OXKI 2/CN
E12     1      OXKIL/CN

```

=> s E3=E4

NUMERIC VALUE NOT VALID '"OXITROPIUM BROMIDE"'

Numeric values may contain 1-8 significant figures. If range notation is used, both the beginning and the end of the range must be specified, e.g., '250-300/MW'. Expressions such as '250-/MW' are not allowed. To search for values above or below a given number, use the >, =>, <, or <= operators, e.g., 'MW => 250'. Text terms cannot be used in numeric expressions. If you specify a unit, it must be dimensionally correct for that field code. To see the unit designations for field codes in the current file, enter "DISPLAY UNIT ALL" at an arrow prompt (=>).

=> s E3-E4

```

1 OXITROPIUM/CN
1 "OXITROPIUM BROMIDE"/CN
L2      2 (OXITROPIUM/CN OR "OXITROPIUM BROMIDE"/CN)

```

=> d 12

L2 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN

RN 99571-64-9 REGISTRY

ED Entered STN: 28 Dec 1985

CN 3-Oxa-9-azoniatricyclo[3.3.1.02,4]nonane, 9-ethyl-7-[(2S)-3-hydroxy-1-oxo-2-phenylpropoxy]-9-methyl-, (1 $\alpha$ ,2 $\beta$ ,4 $\beta$ ,5 $\alpha$ ,7 $\beta$ ) - (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 3-Oxa-9-azatricyclo[3.3.1.02,4]nonane, 3-oxa-9-azoniatricyclo[3.3.1.02,4]nonane deriv.

CN 3-Oxa-9-azoniatricyclo[3.3.1.02,4]nonane, 9-ethyl-7-(3-hydroxy-1-oxo-2-phenylpropoxy)-9-methyl-, [7(S)-(1 $\alpha$ ,2 $\beta$ ,4 $\beta$ ,5 $\alpha$ ,7 $\beta$ ) - ] -

OTHER NAMES:

CN Oxitropium

FS STEREOSEARCH

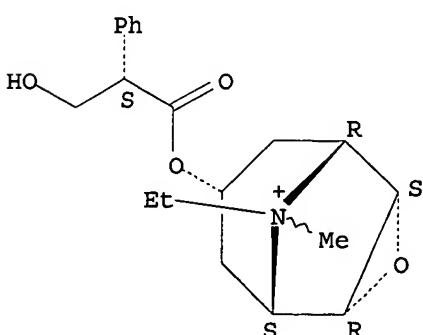
MF C19 H26 N O4

CI COM

SR CA

LC STN Files: BIOSIS, CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.



47 REFERENCES IN FILE CA (1907 TO DATE)  
 15 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 48 REFERENCES IN FILE CAPLUS (1907 TO DATE)

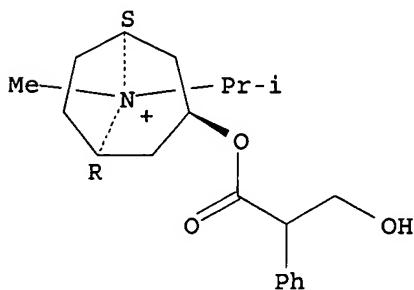
=> exp ipratropium/cn  
 E1 1 IPRAL SODIUM/CN  
 E2 1 IPRAMIDIL/CN  
 E3 1 --> IPRATROPIUM/CN  
 E4 1 IPRATROPIUM BROMIDE/CN  
 E5 1 IPRAVACAINE/CN  
 E6 1 IPRAZID/CN  
 E7 1 IPRAZIDE/CN  
 E8 1 IPRAZOCHROME/CN  
 E9 1 IPRECYNIUM 22/CN  
 E10 1 IPREN/CN  
 E11 1 IPRIFLAVONE/CN  
 E12 1 IPRIFLAVONE-A-CYCLODEXTRIN COMPLEX (1:2)/CN

=> s E3-E4  
 1 IPRATROPIUM/CN  
 1 "IPRATROPIUM BROMIDE"/CN  
 L3 2 (IPRATROPIUM/CN OR "IPRATROPIUM BROMIDE"/CN)

=> d 13

L3 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN  
 RN 60205-81-4 REGISTRY  
 ED Entered STN: 16 Nov 1984  
 CN 8-Azoniarbicyclo[3.2.1]octane, 3-(3-hydroxy-1-oxo-2-phenylpropoxy)-8-methyl-8-(1-methylethyl)-, (3-endo,8-syn)- (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 8-Azoniarbicyclo[3.2.1]octane, 3-(3-hydroxy-1-oxo-2-phenylpropoxy)-8-methyl-8-(1-methylethyl)-, (endo,syn)- (±)-  
 OTHER NAMES:  
 CN (±)-Ipratropine  
 CN 8-Azoniarbicyclo[3.2.1]octane, 3-(3-hydroxy-1-oxo-2-phenylpropoxy)-8-methyl-8-(1-methylethyl)-, (endo,syn)-  
 CN Ipratropium  
 FS STEREOSEARCH  
 DR 197647-02-2  
 MF C20 H30 N O3  
 CI COM  
 LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOSIS, CA, CAPLUS, CBNB, CIN, IMSPATENTS, IPA, MEDLINE, PROMT, RTECS\*, TOXCENTER, USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)

Relative stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

196 REFERENCES IN FILE CA (1907 TO DATE)  
20 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
198 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s cliomilast/cn  
L4 0 CLIOMILAST/CN

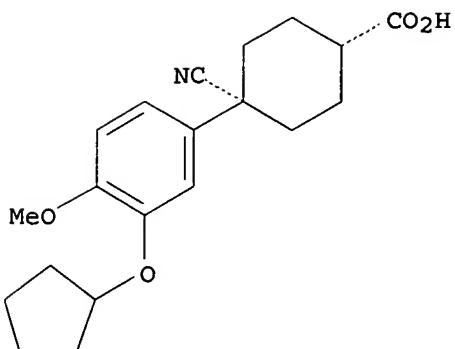
=> exp ariflo/cn  
E1 1 ARIETIN (DISINTEGRIN) /CN  
E2 1 ARIFEN/CN  
E3 1 --> ARIFLO/CN  
E4 1 ARIGAL C/CN  
E5 1 ARIH1 PROTEIN (MOUSE STRAIN FVB/N CLONE MGC:68355 IMAGE:3498  
094)/CN  
E6 1 ARILAT/CN  
E7 1 ARILATE/CN  
E8 1 ARILDONE/CN  
E9 1 ARILID/CN  
E10 1 ARILIN/CN  
E11 1 ARILLANIN A/CN  
E12 1 ARILLANIN B/CN

=> s ariflo/cn  
L5 1 ARIFLO/CN

=> d 15

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN  
RN 153259-65-5 REGISTRY  
ED Entered STN: 24 Feb 1994  
CN Cyclohexanecarboxylic acid, 4-cyano-4-[3-(cyclopentyloxy)-4-methoxyphenyl]-  
, cis- (9CI) (CA INDEX NAME)  
OTHER NAMES:  
CN Ariflo  
CN Cilomilast  
CN cis-4-Cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)cyclohexanecarboxylic acid  
CN cis-4-[3-(Cyclopentyloxy)-4-methoxyphenyl]-4-cyanocyclohexane-1-carboxylic  
acid  
CN SB 207499  
FS STEREOSEARCH  
MF C20 H25 N O4  
CI COM  
SR CA  
LC STN Files: ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CA, CAPLUS,  
CASREACT, CIN, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MRCK\*,  
PHAR, PROMT, PROUSDDR, RTECS\*, SYNTHLINE, TOXCENTER, USAN, USPAT2,  
USPATFULL  
(\*File contains numerically searchable property data)

Relative stereochemistry.



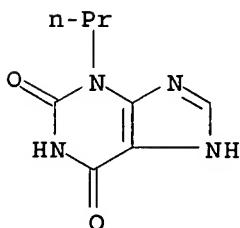
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

200 REFERENCES IN FILE CA (1907 TO DATE)  
 6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 201 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s enprofylline/cn  
 L6 1 ENPROFYLLINE/CN

=> d 16

L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN  
 RN 41078-02-8 REGISTRY  
 ED Entered STN: 16 Nov 1984  
 CN 1H-Purine-2,6-dione, 3,7-dihydro-3-propyl- (9CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN 3-Propylxanthine  
 CN D 4028  
 CN Enprofylline  
 FS 3D CONCORD  
 MF C8 H10 N4 O2  
 LC STN Files: ADISINSIGHT, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOSIS,  
 BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, DDFU,  
 DRUGU, EMBASE, IPA, MEDLINE, PHAR, PROMT, PROUSDDR, RTECS\*, SYNTHLINE,  
 TOXCENTER, USAN, USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)  
 Other Sources: EINECS\*\*, WHO  
 (\*\*Enter CHEMLIST File for up-to-date regulatory information)



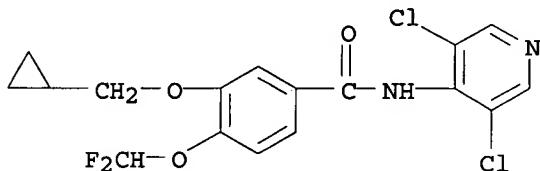
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

304 REFERENCES IN FILE CA (1907 TO DATE)  
 6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 304 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=> s roflumilast/cn
L7      1 ROFLUMILAST/CN
```

```
=> d 17
```

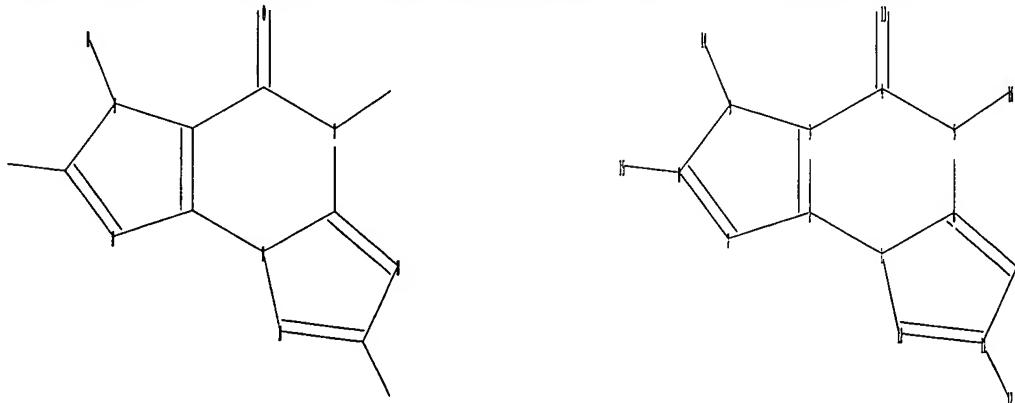
```
L7  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2006 ACS on STN
RN  162401-32-3  REGISTRY
ED  Entered STN: 21 Apr 1995
CN  Benzamide, 3-(cyclopropylmethoxy)-N-(3,5-dichloro-4-pyridinyl)-4-
     (difluoromethoxy)- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN  B 9302-107
CN  BY 217
CN  BYK 20869
CN  Roflumilast
FS  3D CONCORD
MF  C17 H14 Cl2 F2 N2 O3
CI  COM
SR  CA
LC  STN Files: ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CA, CAPLUS,
     CASREACT, CBNB, CHEMCATS, CIN, DDFU, DRUGU, EMBASE, IMSDRUGNEWS,
     IMSPATENTS, IMSRESEARCH, IPA, MRCK*, PHAR, PROMT, PROUSDDR, RTECS*,
     SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
     (*File contains numerically searchable property data)
```



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

138 REFERENCES IN FILE CA (1907 TO DATE)  
11 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
139 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=>
Uploading C:\Program Files\Stnexp\Queries\10613783pde4.str
```



```
chain nodes :
13 14 15 16 17
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12
```

```

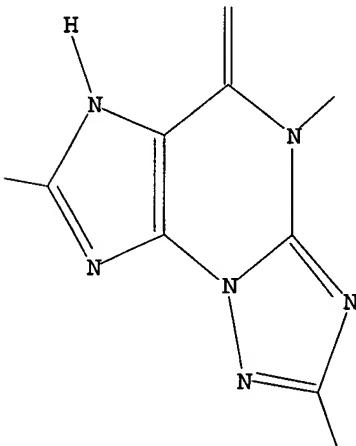
chain bonds :
4-13 5-16 8-15 9-14 11-17
ring bonds :
1-2 1-6 1-12 2-3 2-7 3-4 3-9 4-5 5-6 6-10 7-8 8-9 10-11 11-12
exact/norm bonds :
1-2 1-6 1-12 2-3 2-7 3-4 3-9 4-5 4-13 5-6 5-16 6-10 7-8 8-9 10-11
11-12
exact bonds :
8-15 9-14 11-17

```

Match level :  
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS

L8 STRUCTURE UPLOADED

=> d 18  
L8 HAS NO ANSWERS  
L8 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 18  
SAMPLE SEARCH INITIATED 15:03:47 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 6 TO ITERATE

100.0% PROCESSED      6 ITERATIONS      0 ANSWERS  
SEARCH TIME: 00:00:01

FULL FILE PROJECTIONS:	ONLINE	**COMPLETE**	
	BATCH	**COMPLETE**	
PROJECTED ITERATIONS:	6	TO	266
PROJECTED ANSWERS:	0	TO	0

L9 0 SEA SSS SAM L8

```
=> s 18 sss full
FULL SEARCH INITIATED 15:03:52 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 174 TO ITERATE
```

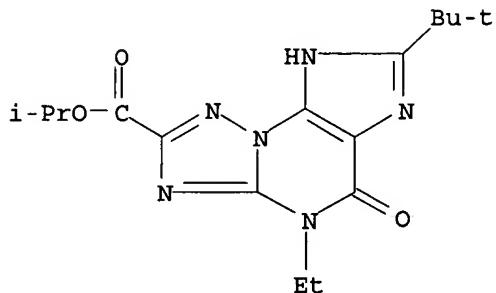
100.0% PROCESSED 174 ITERATIONS 23 ANSWERS  
SEARCH TIME: 00.00.01

L10

23 SEA SSS FUL L8

=> d 110 scan

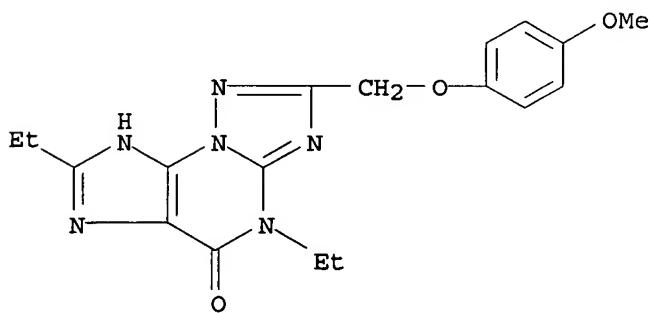
L10 23 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
IN 4H-[1,2,4]Triazolo[5,1-b]purine-2-carboxylic acid, 7-(1,1-dimethylethyl)-4-ethyl-5,6-dihydro-5-oxo-, 1-methylethyl ester (9CI)  
MF C16 H22 N6 O3



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

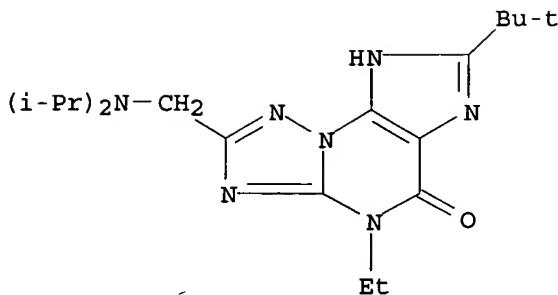
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L10 23 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
IN 4H-[1,2,4]Triazolo[5,1-b]purin-5(6H)-one, 4,7-diethyl-2-[(4-methoxyphenoxy)methyl]- (9CI)  
MF C18 H20 N6 O3



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L10 23 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN  
IN 4H-[1,2,4]Triazolo[5,1-b]purin-5(6H)-one, 2-[[bis(1-methylethyl)amino]methyl]-7-(1,1-dimethylethyl)-4-ethyl- (9CI)  
MF C19 H31 N7 O



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1): 0

FILE 'CAPLUS' ENTERED AT 15:04:11 ON 22 AUG 2006  
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FILE COVERS 1907 - 22 Aug 2006 VOL 145 ISS 9  
FILE LAST UPDATED: 21 Aug 2006 (20060821/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

=> d his

(FILE 'HOME' ENTERED AT 14:59:11 ON 22 AUG 2006)

FILE 'REGISTRY' ENTERED AT 14:59:37 ON 22 AUG 2006  
EXP. TIOTROPIUM/CN

L1	10	S E3-E12
		EXP OXATROPIUM/CN
		EXP OXITROPIUM/CN
L2	2	S E3-E4
		EXP IPRATROPIUM/CN
L3	2	S E3-E4
L4	0	S CLIOMILAST/CN
		EXP ARIFLO/CN
L5	1	S ARIFLO/CN
L6	1	S ENPROFYLLINE/CN

L7 1 S ROFLUMILAST/CN  
L8 STRUCTURE uploaded  
L9 0 S L8  
L10 23 S L8 SSS FULL

FILE 'CAPLUS' ENTERED AT 15:04:11 ON 22 AUG 2006

=> s L1 or L2 or L3  
270 L1  
167 L2  
705 L3  
L11 881 L1 OR L2 OR L3

=> s L5 or L6 or L7 or L10  
201 L5  
304 L6  
139 L7  
5 L10  
L12 556 L5 OR L6 OR L7 OR L10

=> s L11 and L12  
L13 26 L11 AND L12

=> `s L13 and (asthma or COPD or (chronic(w)obstructive(w)pulmonary(w)disease))  
0 ASTHSMA  
2718 COPD  
201254 CHRONIC  
11037 OBSTRUCTIVE  
83467 PULMONARY  
880139 DISEASE  
5289 CHRONIC(W)OBSTRUCTIVE(W)PULMONARY(W)DISEASE  
L14 10 L13 AND (ASTHSMA OR COPD OR (CHRONIC(W)OBSTRUCTIVE(W)PULMONARY(W)  
)DISEASE))

=> s l14 not py>2001  
5196001 PY>2001  
L15 0 L14 NOT PY>2001

=> s l14 not py>2002  
4216904 PY>2002  
L16 0 L14 NOT PY>2002

=> s L11 and (asthma or COPD or (chronic(w)obstructive(w)pulmonary(w)disease))  
0 ASTHSMA  
2718 COPD  
201254 CHRONIC  
11037 OBSTRUCTIVE  
83467 PULMONARY  
880139 DISEASE  
5289 CHRONIC(W)OBSTRUCTIVE(W)PULMONARY(W)DISEASE  
L17 237 L11 AND (ASTHSMA OR COPD OR (CHRONIC(W)OBSTRUCTIVE(W)PULMONARY(W)  
)DISEASE))

=> s l17 not py>2001  
5196001 PY>2001  
L18 51 L17 NOT PY>2001

=> d l18 1-18 ti

L18 ANSWER 1 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Asthma medications and their potential adverse effects in the elderly:  
Recommendations for prescribing

L18 ANSWER 2 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Pharmacokinetics and tissue distribution of the anticholinergics

tiotropium and ipratropium in the rat and dog

L18 ANSWER 3 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Ipratropium bromide hydrofluoroalkane inhalation aerosol is safe and effective in patients with COPD

L18 ANSWER 4 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Effective delivery of particles with the HandiHaler dry powder inhalation system over a range of chronic obstructive pulmonary disease severity

L18 ANSWER 5 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Management of acute exacerbations of chronic obstructive pulmonary disease

L18 ANSWER 6 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Effectiveness of salmeterol versus ipratropium bromide on exertional dyspnea in COPD

L18 ANSWER 7 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Inhaled salmeterol: A review of its efficacy in chronic obstructive pulmonary disease

L18 ANSWER 8 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN  
TI In patients with COPD, treatment with a combination of formoterol and ipratropium is more effective than a combination of salbutamol and ipratropium: A 3-week, randomized, double-blind, within-patient, multicenter study

L18 ANSWER 9 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Antimuscarinic treatment for lung diseases. From research to clinical practice

L18 ANSWER 10 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Anticholinergics: Tiotropium

L18 ANSWER 11 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Tiotropium bromide

L18 ANSWER 12 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Systemic glucocorticoids in severe exacerbations of COPD

L18 ANSWER 13 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Effect of ipratropium bromide on airway and pulmonary muscarinic receptors in a rat model of chronic obstructive pulmonary disease

L18 ANSWER 14 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN  
TI The impact of combined inhaled bronchodilator therapy in the treatment of COPD

L18 ANSWER 15 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Inhaled anticholinergic therapy: applied pharmacology and interesting developments

L18 ANSWER 16 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Anticholinergic bronchodilators in combination

L18 ANSWER 17 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Tiotropium bromide: treatment of COPD, bronchodilator, muscarinic antagonist

L18 ANSWER 18 OF 51 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Long-term treatment of chronic obstructive pulmonary disease with salmeterol and the additive

effect of ipratropium

=> s l18 and tiotropium

289 TIOTROPIUM

L19 11 L18 AND TIOTROPIUM

=> d l19 1-11 ti

L19 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Pharmacokinetics and tissue distribution of the anticholinergics tiotropium and ipratropium in the rat and dog

L19 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Effective delivery of particles with the HandiHaler dry powder inhalation system over a range of chronic obstructive pulmonary disease severity

L19 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Antimuscarinic treatment for lung diseases. From research to clinical practice

L19 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Anticholinergics: Tiotropium

L19 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Tiotropium bromide

L19 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Inhaled anticholinergic therapy: applied pharmacology and interesting developments

L19 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Tiotropium bromide: treatment of COPD, bronchodilator, muscarinic antagonist

L19 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Tiotropium (Ba 679): Pharmacology and early clinical observations

L19 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Tiotropium (Spiriva): mechanistical considerations and clinical profile in obstructive lung disease

L19 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Tiotropium bromide, a new long-acting antimuscarinic bronchodilator: a pharmacodynamic study in patients with chronic obstructive pulmonary disease (COPD)

L19 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

TI Tiotropium bromide (Ba 679 BR), a novel long-acting muscarinic antagonist for the treatment of obstructive airways disease

=> d l19 1 2 4 5 6 7 8 9 10 11

L19 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2001:936981 CAPLUS

DN 136:210019

TI Pharmacokinetics and tissue distribution of the anticholinergics tiotropium and ipratropium in the rat and dog

AU Leusch, A.; Eichhorn, B.; Muller, G.; Rominger, K.-L.

CS Department of Pharmacokinetics and Drug Metabolism, Boehringer Ingelheim Pharma KG, Biberach, 88397, Germany

SO Biopharmaceutics & Drug Disposition (2001), 22(5), 199-212

CODEN: BDDID8; ISSN: 0142-2782  
PB John Wiley & Sons Ltd.  
DT Journal  
LA English  
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 2001:689613 CAPLUS  
DN 136:390861  
TI Effective delivery of particles with the HandiHaler dry powder inhalation system over a range of chronic obstructive pulmonary disease severity  
AU Chodosh, Sanford; Flanders, Judith S.; Kesten, Steven; Serby, Charles W.; Hochrainer, Dieter; Witek, Theodore J., Jr.  
CS Veterans Administration Outpatient Clinic, Pulmonary Research, Boston, MA, USA  
SO Journal of Aerosol Medicine (2001), 14(3), 309-315  
CODEN: JAEMEP; ISSN: 0894-2684  
PB Mary Ann Liebert, Inc.  
DT Journal  
LA English  
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 2001:360977 CAPLUS  
DN 135:235691  
TI Anticholinergics: Tiotropium  
AU Disse, Bernd; Witek, Theodore J., Jr.  
CS Clinical Research Institute, Boehringer Ingelheim, Ingelheim/Rhein, Germany  
SO Progress in Respiratory Research (2001), 31(New Drugs for Asthma, Allergy and COPD), 72-76  
CODEN: PRRRAE; ISSN: 1422-2140  
PB S. Karger AG  
DT Journal; General Review  
LA English  
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 2001:266014 CAPLUS  
DN 135:40286  
TI Tiotropium bromide  
AU Barnes, Peter J.  
CS Department of Thoracic Medicine, National Heart and Lung Institute, Imperial College, London, UK  
SO Expert Opinion on Investigational Drugs (2001), 10(4), 733-740  
CODEN: EOIDER; ISSN: 1354-3784  
PB Ashley Publications Ltd.  
DT Journal; General Review  
LA English  
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 2001:65653 CAPLUS  
DN 135:86394  
TI Inhaled anticholinergic therapy: applied pharmacology and interesting developments  
AU Witek, Theodore J., Jr.; Disse, Bernd  
CS Head, Respiratory & Immunology Clinical Research, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, 06877-0363, USA  
SO Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2001), 2(1),

53-58

CODEN: COIDAZ

PB PharmaPress Ltd.

DT Journal; General Review

LA English

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2000:717146 CAPLUS

DN 134:260728

TI Tiotropium bromide: treatment of COPD, bronchodilator, muscarinic antagonist

AU Norman, P.; Graul, A.; Rabasseda, X.; Castaner, J.

CS Bucks, SL1 8JW, UK

SO Drugs of the Future (2000), 25(7), 693-699

CODEN: DRFUD4; ISSN: 0377-8282

PB Prous Science

DT Journal; General Review

LA English

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2000:53706 CAPLUS

DN 132:73121

TI Tiotropium (Ba 679): Pharmacology and early clinical observations

AU Witek, Theodore J., Jr.; Souhrada, Joseph F.; Serby, Charles W.; Disse, Bernd

CS Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA

SO Lung Biology in Health and Disease (1999), 134 (Anticholinergic Agents in the Upper and Lower Airways), 137-152

CODEN: LBHDD7; ISSN: 0362-3181

PB Marcel Dekker, Inc.

DT Journal; General Review

LA English

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1999:87226 CAPLUS

DN 130:261837

TI Tiotropium (Spiriva): mechanistical considerations and clinical profile in obstructive lung disease

AU Disse, Bernd; Speck, Georg A.; Rominger, Karl Ludwig; Witek, Theodore J., Jr.; Hammer, Rudolf

CS Corporate Medical Division and R&D Division, Boehringer Ingelheim, Ingelheim, 55216, Germany

SO Life Sciences (1999), 64(6/7), 457-464

CODEN: LIFSAK; ISSN: 0024-3205

PB Elsevier Science Inc.

DT Journal

LA English

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1995:971815 CAPLUS

DN 124:76095

TI Tiotropium bromide, a new long-acting antimuscarinic bronchodilator: a pharmacodynamic study in patients with chronic obstructive pulmonary disease (COPD)

AU Maesen, F. P. V.; Smeets, J. J.; Sledsens, T. J. H.; Wald, F. D. M.; Cornelissen, P. J. G.

CS Dept. Respiratory Diseases, De Wever Hospital, Heerlen, Neth.  
SO European Respiratory Journal (1995), 8(9), 1506-13  
CODEN: ERJOEI; ISSN: 0903-1936  
PB Munksgaard  
DT Journal  
LA English

L19 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 1995:381396 CAPLUS  
DN 122:151131  
TI Tiotropium bromide (Ba 679 BR), a novel long-acting muscarinic antagonist for the treatment of obstructive airways disease  
AU Barnes, Peter J.; Belvisi, Maria G.; Mak, Judith CW; Haddad, El-Bdaoui; O'Connor, Brian  
CS Dep. Thoracic Med., Natl. Heart Lung Inst., London, SW3 6LY, UK  
SO Life Sciences (1995), 56(11/12), 853-60  
CODEN: LIFSAK; ISSN: 0024-3205  
PB Elsevier  
DT Journal  
LA English

=> s l19 and asthsma  
0 ASTHSMA  
L20 0 L19 AND ASTHSMA

=> s l19 and asthma  
31962 ASTHMA  
L21 3 L19 AND ASTHMA

=> d l21 1-3

L21 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 2001:65653 CAPLUS  
DN 135:86394  
TI Inhaled anticholinergic therapy: applied pharmacology and interesting developments  
AU Witek, Theodore J., Jr.; Disse, Bernd  
CS Head, Respiratory & Immunology Clinical Research, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, 06877-0363, USA  
SO Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2001), 2(1), 53-58  
CODEN: COIDAZ  
PB PharmaPress Ltd.  
DT Journal; General Review  
LA English

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 1999:87226 CAPLUS  
DN 130:261837  
TI Tiotropium (Spiriva): mechanistical considerations and clinical profile in obstructive lung disease  
AU Disse, Bernd; Speck, Georg A.; Rominger, Karl Ludwig; Witek, Theodore J., Jr.; Hammer, Rudolf  
CS Corporate Medical Division and R&D Division, Boehringer Ingelheim, Ingelheim, 55216, Germany  
SO Life Sciences (1999), 64(6/7), 457-464  
CODEN: LIFSAK; ISSN: 0024-3205  
PB Elsevier Science Inc.  
DT Journal  
LA English

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 1995:381396 CAPLUS  
DN 122:151131  
TI Tiotropium bromide (Ba 679 BR), a novel long-acting muscarinic antagonist for the treatment of obstructive airways disease  
AU Barnes, Peter J.; Belvisi, Maria G.; Mak, Judith CW; Haddad, El-Bdaoui; O'Connor, Brian  
CS Dep. Thoracic Med., Natl. Heart Lung Inst., London, SW3 6LY, UK  
SO Life Sciences (1995), 56(11/12), 853-60  
CODEN: LIFSAK; ISSN: 0024-3205  
PB Elsevier  
DT Journal  
LA English

=> s L11 and asthsma and COPD or (chronic(w)obstructive(w)pulmonary(w)disease))  
UNMATCHED RIGHT PARENTHESIS 'DISEASE)'  
The number of right parentheses in a query must be equal to the number of left parentheses.

=> s L12 and asthsma and (COPD or (chronic(w)obstructive(w)pulmonary(w)disease))  
0 ASTHSMA  
2718 COPD  
201254 CHRONIC  
11037 OBSTRUCTIVE  
83467 PULMONARY  
880139 DISEASE  
5289 CHRONIC(W)OBSTRUCTIVE(W)PULMONARY(W)DISEASE  
L22 0 L12 AND ASTHSMA AND (COPD OR (CHRONIC(W)OBSTRUCTIVE(W)PULMONARY(W)DISEASE))

=> s L12 and (COPD or (chronic(w)obstructive(w)pulmonary(w)disease))  
2718 COPD  
201254 CHRONIC  
11037 OBSTRUCTIVE  
83467 PULMONARY  
880139 DISEASE  
5289 CHRONIC(W)OBSTRUCTIVE(W)PULMONARY(W)DISEASE  
L23 85 L12 AND (COPD OR (CHRONIC(W)OBSTRUCTIVE(W)PULMONARY(W)DISEASE))

=> s l23 not py>2001  
5196001 PY>2001  
L24 14 L23 NOT PY>2001

=> d l24 1-14 ti

L24 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Warfarin pharmacodynamics unaffected by cilomilast  
L24 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Cilomilast, a selective phosphodiesterase-4 inhibitor for treatment of patients with chronic obstructive pulmonary disease: a randomised, dose-ranging study  
L24 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI The next generation of PDE4 inhibitors  
L24 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Cilomilast: a second generation phosphodiesterase 4 inhibitor for asthma and chronic obstructive pulmonary disease  
L24 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI In vivo efficacy in airway disease models of roflumilast, a novel orally

active PDE4 inhibitor

L24 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Anti-inflammatory and immunomodulatory potential of the novel PDE4 inhibitor roflumilast in vitro

L24 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Roflumilast: antiallergy/antiasthmatic, treatment of COPD, phosphodiesterase 4 inhibitor

L24 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Chronic obstructive pulmonary disease: emerging therapies

L24 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Low-adenosine antisense oligonucleotide agents, compositions, kits and treatments for respiratory disorders

L24 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Ariflo SmithKline Beecham

L24 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Ariflo SmithKline Beecham plc

L24 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI AriflotM(SB 207499), a second generation phosphodiesterase 4 inhibitor for the treatment of asthma and COPD: from concept to clinic

L24 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI SB-207499 SmithKline Beecham plc

L24 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI SB-207499. antiasthmatic/antiinflammatory, phosphodiesterase IV inhibitor

=> d 124 2 4 5 6 7 8 10 11 12 13 14 ti abs bib

L24 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Cilomilast, a selective phosphodiesterase-4 inhibitor for treatment of patients with chronic obstructive pulmonary disease: a randomised, dose-ranging study

AB Background Chronic obstructive pulmonary disease (COPD) is a common, progressive respiratory disease that causes great morbidity and mortality despite treatment. There is evidence for airway inflammation in COPD. Cilomilast is an orally active, potent, selective phosphodiesterase type 4 inhibitor, which in vitro can affect cells thought to be of clin. importance in COPD. The authors' aim was to assess the safety, efficacy, and dose response of cilomilast in the treatment of patients with this disease. Methods The authors did a 6-wk, randomized, dose-ranging study in 424 patients with COPD (forced expiratory volume in 1 s [FEV1] 46.8% of predicted, FEV1/forced vital capacity [FVC] 54.6%, and postsalbutamol reversibility 5.4%). The authors randomly assigned individuals at 60 European centers to receive cilomilast 5 (n=109), 10 (n=102), or 15 (n=107) mg twice daily, or placebo (n=106). The main outcome measure was trough FEV1 before and after use of a bronchodilator. Analyses were by intention to treat. Findings Cilomilast 15 mg twice daily significantly improved FEV1 compared with placebo (mean 130 mL vs -30 mL [95% CI 90-240] at week 6). FVC and peak expiratory flow were also improved. Quality of life measures did not differ significantly between the groups. There were no significant differences in serious adverse events between the groups. Interpretation Cilomilast 15 mg twice daily might be an effective maintenance treatment for COPD. Further clin. studies are underway.

AN 2001:574024 CAPLUS

DN 136:319139  
TI Cilomilast, a selective phosphodiesterase-4 inhibitor for treatment of patients with chronic obstructive pulmonary disease: a randomised, dose-ranging study  
AU Compton, C. H.; Gubb, J.; Nieman, R.; Edelson, J.; Amit, O.; Bakst, A.; Ayres, J. G.; Creemers, J. P. H. M.; Schultze-Werninghaus, G.; Brambilla, C.; Barnes, N. C.  
CS International Study Group, Department of SmithKline Beecham Pharmaceuticals, Harlow, UK  
SO Lancet (2001), 358(9278), 265-270  
CODEN: LANCAO; ISSN: 0140-6736  
PB Lancet Ltd.  
DT Journal  
LA English

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Cilomilast: a second generation phosphodiesterase 4 inhibitor for asthma and chronic obstructive pulmonary disease  
AB A review with 126 refs. Cilomilast (Ariflo, SB-207499) is an orally-active, second generation phosphodiesterase (PDE) inhibitor that may be effective in the treatment of asthma and chronic obstructive pulmonary disease (COPD). It has high selectivity for the cAMP-specific, or PDE4, isoenzyme that predominates in pro-inflammatory and immune cells and is ten-fold more selective for PDE4D than for PDE4A, B and C. In vitro, cilomilast suppresses the activity of many pro-inflammatory and immune cells that have been implicated in the pathogenesis of asthma and COPD and is highly active in animal models of these diseases. Cilomilast demonstrates a markedly improved side effect profile over the archetypal PDE4 inhibitor, rolipram, which has been attributed to its inability to discriminate between the high affinity rolipram binding site and the catalytic domain of the enzyme, and the fact that it is neg. charged which at physiol. pH should limit its penetration in to the CNS. In humans cilomilast is rapidly absorbed after oral administration, providing dose-proportional systemic exposure up to 4 mg, completely bioavailable, has a half-life of .apprx. 7 h and is subject to negligible first pass hepatic metabolism. Cilomilast is extensively metabolized with decyclopentylation, acyl glucuronidation and 3-hydroxylation of the cyclopentyl ring representing the principal routes. Most of the drug is excreted in the urine (.apprx. 90%) and feces (6 - 7%) with unchanged cilomilast accounting for less than 1% of the administered dose. Cilomilast has been evaluated in Phase I, Phase II and Phase III trials and dose-response expts. have demonstrated a clin. significant increase in lung function and a perceived improvement in quality of life in patients with COPD. Trials of cilomilast in asthma have been less impressive although a trend towards improved lung function has been reported. Cilomilast is safe and well-tolerated at doses up to 15 mg in both short- and long-term dosing trials with a low incidence of adverse effects. No evidence for drug-drug interactions with commonly prescribed medications for COPD and asthma such as digoxin, corticosteroids, salbutamol, theophylline or warfarin has been found. Moreover, the pharmacokinetics of cilomilast are essentially the same in smokers and non-smokers, indicating that no dose adjustments of cilomilast will be required in patients with COPD. Thus, cilomilast displays a promising clin. profile in the treatment of inflammatory airway diseases, in particular COPD and the results of further Phase III trials are awaited with interest.

AN 2001:522203 CAPLUS

DN 135:220550

TI Cilomilast: a second generation phosphodiesterase 4 inhibitor for asthma and chronic obstructive pulmonary disease

AU Giembycz, Mark A.  
CS Thoracic Medicine, National Heart & Lung Institute, Imperial College School of Medicine, London, UK  
SO Expert Opinion on Investigational Drugs (2001), 10(7), 1361-1379  
CODEN: EOIDER; ISSN: 1354-3784  
PB Ashley Publications Ltd.  
DT Journal; General Review  
LA English

RE.CNT 127 THERE ARE 127 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI In vivo efficacy in airway disease models of roflumilast, a novel orally active PDE4 inhibitor  
AB We have investigated the bronchodilator and anti-inflammatory properties of roflumilast (3-cyclopropylmethoxy-4-difluoromethoxy-N-[3,5-dichloropyrid-4-yl]-benzamide), a novel, highly potent, and selective phosphodiesterase 4 (PDE4) inhibitor. Addnl., we compared the effects of roflumilast and its N-oxide, the primary metabolite in vivo, with those of the PDE4 inhibitors piclamilast, rolipram, and cilomilast. Roflumilast inhibited the ovalbumin-evoked contractions of tracheal chains prepared from sensitized guinea pigs ( $EC_{50} = 2.10^{-7}$  M) but showed no relaxant effect on tissues contracted spontaneously. In spasmogen-challenged rats and guinea pigs, i.v. administered roflumilast displayed bronchodilatory activity ( $ED_{50} = 4.4$  and  $7.1 \mu\text{mol/kg}$ , resp.). Furthermore, roflumilast dose dependently attenuated allergen-induced bronchoconstriction in guinea pigs ( $ED_{50} = 0.1 \mu\text{mol/kg}$  i.v.). Roflumilast given orally ( $ED_{50} = 1.5 \mu\text{mol/kg}$ ) showed equal potency to its N-oxide ( $ED_{50} = 1.0 \mu\text{mol/kg}$ ) but was superior to piclamilast ( $ED_{50} = 8.3 \mu\text{mol/kg}$ ), rolipram ( $ED_{50} = 32.5 \mu\text{mol/kg}$ ), and cilomilast ( $ED_{50} = 52.2 \mu\text{mol/kg}$ ) in suppressing allergen-induced early airway reactions. To assess the anti-inflammatory potential of orally administered roflumilast, antigen-induced cell infiltration, total protein, and  $\text{TNF}\alpha$  concentration in bronchoalveolar lavage fluid of Brown Norway rats were determined. Roflumilast and its N-oxide equally inhibited eosinophilia ( $ED_{50} = 2.7$  and  $2.5 \mu\text{mol/kg}$ , resp.), whereas the reference inhibitors displayed lower potency ( $ED_{50} = 17-106 \mu\text{mol/kg}$ ). Besides, orally administered roflumilast abrogated LPS-induced circulating  $\text{TNF}\alpha$  in the rat ( $ED_{50} = 0.3 \mu\text{mol/kg}$ ), an effect shared by its N-oxide, with both mols. exhibiting 8-, 25-, and 310-fold superiority to piclamilast, rolipram, and cilomilast, resp. These results, coupled with the in vitro effects of roflumilast on inflammatory cells, suggest that roflumilast represents a potential new drug for the treatment of asthma and chronic obstructive pulmonary disease.

AN 2001:240840 CAPLUS  
DN 135:86928  
TI In vivo efficacy in airway disease models of roflumilast, a novel orally active PDE4 inhibitor  
AU Bundschuh, Daniela S.; Eltze, Manfrid; Barsig, Johannes; Wollin, Lutz; Hatzelmann, Armin; Beume, Rolf  
CS Department of Pharmacology, Byk Gulden, Konstanz, Germany  
SO Journal of Pharmacology and Experimental Therapeutics (2001), 297(1), 280-290  
CODEN: JPETAB; ISSN: 0022-3565  
PB American Society for Pharmacology and Experimental Therapeutics  
DT Journal  
LA English

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Anti-inflammatory and immunomodulatory potential of the novel PDE4 inhibitor roflumilast in vitro  
AB From a series of benzamide derivs., roflumilast (3-cyclopropylmethoxy-4-difluoromethoxy-N-[3,5-di-chloropyrid-4-yl]benzamide) was identified as a

potent and selective PDE4 inhibitor. It inhibits PDE4 activity from human neutrophils with an IC<sub>50</sub> of 0.8 nM without affecting PDE1 (bovine brain), PDE2 (rat heart), and PDE3 and PDE5 (human platelets) even at 10,000-fold higher concns. Roflumilast is almost equipotent to its major metabolite formed in vivo (roflumilast N-oxide) and piclamilast (RP 73401), however, more than 100-fold more potent than rolipram and Ariflo (cilmilast; SB 207499). The anti-inflammatory and immunomodulatory potential of roflumilast and the reference compds. was investigated in various human leukocytes using cell-specific responses: neutrophils [N-formyl-methyl-leucyl-phenylalanine (fMLP)-induced formation of LTB4 and reactive oxygen species (ROS)], eosinophils (fMLP- and C5a-induced ROS formation), monocytes, monocyte-derived macrophages, and dendritic cells (lipopolysaccharide-induced tumor necrosis factor- $\alpha$  synthesis), and CD4+ T cells (anti-CD3/anti-CD28 monoclonal antibody-stimulated proliferation, IL-2, IL-4, IL-5, and interferon- $\gamma$  release). Independent of the cell type and the response investigated, the corresponding IC values (for half-maximum inhibition) of roflumilast were within a narrow range (2-21 nM), very similar to roflumilast N-oxide (3-40 nM) and piclamilast (2-13 nM). In contrast, cilmilast (40-3000 nM) and rolipram (10-600 nM) showed greater differences with the highest potency for neutrophils. Compared with neutrophils and eosinophils, representing the terminal inflammatory effector cells, the relative potency of roflumilast and its N-oxide for monocytes, CD4+ T cells, and dendritic cells is substantially higher compared with cilmilast and rolipram, probably reflecting an improved immunomodulatory potential. The efficacy of roflumilast in vitro and in vivo (see accompanying article in this issue) suggests that roflumilast will be useful in the treatment of chronic inflammatory disorders such as asthma and chronic obstructive pulmonary disease.

AN 2001:240839 CAPLUS  
DN 135:28819  
TI Anti-inflammatory and immunomodulatory potential of the novel PDE4 inhibitor roflumilast in vitro  
AU Hatzelmann, Armin; Schudt, Christian  
CS Department of Biochemistry, Byk Gulden, Konstanz, Germany  
SO Journal of Pharmacology and Experimental Therapeutics (2001), 297(1), 267-279  
CODEN: JPETAB; ISSN: 0022-3565  
PB American Society for Pharmacology and Experimental Therapeutics  
DT Journal  
LA English  
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Roflumilast: antiallergy/antiasthmatic, treatment of COPD, phosphodiesterase 4 inhibitor  
AB A review with 16 refs. regarding the drug roflumilast which is used to treat chronic obstructive pulmonary disease (COPD) and asthma. Topics discussed include its synthesis, description, pharmacol. actions, and clin. studies.  
AN 2001:196352 CAPLUS  
DN 135:161992  
TI Roflumilast: antiallergy/antiasthmatic, treatment of COPD, phosphodiesterase 4 inhibitor  
AU Sorbera, L. A.; Leeson, P. A.; Castaner, J.  
CS Prous Science, Barcelona, 08080, Spain  
SO Drugs of the Future (2000), 25(12), 1261-1264  
CODEN: DRFUD-; ISSN: 0377-8282  
PB Prous Science  
DT Journal; General Review  
LA English  
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Chronic obstructive pulmonary disease: emerging therapies  
AB A review with 60 refs. Despite the high prevalence of and mortality from chronic obstructive pulmonary disease , extensive research on the underlying pathophysiol. and specific therapeutics for this disease is, relatively, in its infancy. Several novel mol. targets are being investigated as potential treatments for the disease. The most exciting new class of compds. is the phosphodiesterase 4 inhibitors; Ariflo (SB 207499) - a member of this class, and the most advanced in development (Phase III) - was reported recently to have significant clin. efficacy in patients with chronic obstructive pulmonary disease.

Phosphodiesterase 4 inhibitors, such as Ariflo, possibly represent the most important advance in pulmonary medicine in recent years.

AN 2000:584132 CAPLUS  
DN 133:246695  
TI Chronic obstructive pulmonary disease: emerging therapies  
AU Hay, Douglas W. P.  
CS Department of Pulmonary Biology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA  
SO Current Opinion in Chemical Biology (2000), 4(4), 412-419  
CODEN: COCBF4; ISSN: 1367-5931  
PB Elsevier Science Ltd.  
DT Journal; General Review  
LA English

RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Ariflo SmithKline Beecham  
AB A review with .apprx.120 refs. Ariflo (SB-207499) is a phosphodiesterase (PDE)4 inhibitor under development by SmithKline Beecham and in phase III and II clin. trials as a potential treatment for chronic obstructive pulmonary disease (COPD) and asthma, resp. It has commenced phase II trials as a treatment for bronchial asthma in Japan. In Feb. 1999, Merrill Lynch predicted that Ariflo would be launched by the end of 2000 or early 2001 with first year sales of UK £25 million rising to UK £175 million in 2003. In July 1999, Merrill Lynch forecast filing of Ariflo by the second half of 2000. In Feb. 1999, ABN Amro predicted sales of UK £52 million in 2001, rising to UK £254 million in 2005.

AN 1999:732844 CAPLUS  
DN 132:202457  
TI Ariflo SmithKline Beecham  
AU Brown, William  
CS Somerville, NJ, 08876-8139, USA  
SO Current Opinion in Cardiovascular, Pulmonary & Renal Investigational Drugs (1999), 1(4), 506-515  
CODEN: CCPRFX; ISSN: 1464-8482  
PB Current Drugs Ltd.  
DT Journal; General Review  
LA English

RE.CNT 157 THERE ARE 157 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Ariflo SmithKline Beecham plc  
AB A review with 136 refs. Ariflo (SB-207499) is a phosphodiesterase (PDE)4 inhibitor under development by SmithKline Beecham and in phase III and II clin. trials as a potential treatment for chronic obstructive pulmonary disease (COPD) and asthma, resp. [284490]. It has commenced phase II trials as a treatment for bronchial asthma in Japan [248285,300145]. In Feb. 1999,

Merrill Lynch predicted that Ariflo would be launched by the end of 2000 or early 2001 with first year sales of UK £25 million rising to UK £175 million in 2003 [300257, 314372]. In Feb. 1999 ABN Amro predicted sales of UK £52 million in 2001 rising to UK £254 million in 2005 [317577, 328676].

AN 1999:609466 CAPLUS  
DN 131:222870  
TI Ariflo SmithKline Beecham plc  
AU Brown, William  
CS Somerville, NJ, 08876-8139, USA  
SO IDRugs (1999), 2(9), 915-924  
CODEN: IDRUFN; ISSN: 1369-7056  
PB Current Drugs Ltd.  
DT Journal; General Review  
LA English

RE.CNT 135 THERE ARE 135 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI AriflotM(SB 207499), a second generation phosphodiesterase 4 inhibitor for the treatment of asthma and COPD: from concept to clinic  
AB A review with 22 refs. on efficacy and safety of the title PDE4 inhibitor in the treatment of pulmonary diseases. (c) 1999 Academic Press.  
AN 1999:387455 CAPLUS  
DN 131:222898  
TI AriflotM(SB 207499), a second generation phosphodiesterase 4 inhibitor for the treatment of asthma and COPD: from concept to clinic  
AU Torphy, T. J.; Barnette, M. S.; Underwood, D. C.; Griswold, D. E.; Christensen, S. B.; Murdoch, R. D.; Nieman, R. B.; Compton, C. H.  
CS Division of Cardiovascular and Pulmonary Research, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA  
SO Pulmonary Pharmacology & Therapeutics (1999), 12(2), 131-135  
CODEN: PPTHFJ; ISSN: 1094-5539  
PB Academic Press  
DT Journal; General Review  
LA English

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI SB-207499 SmithKline Beecham plc  
AB A review with many refs. SB-207499 (Ariflo) is a phosphodiesterase type 4 (PDE4) inhibitor under development by SmithKline Beecham; the drug is in phase III and II clin. trials as a potential treatment for chronic obstructive pulmonary disease (COPD) and asthma, resp. The company has also begun phase II trials as a treatment for bronchial asthma in Japan. In Feb. 1999 Merrill Lynch predicted that Ariflo would be launched by the end of 2000 or early 2001 with first year sales of STG 25 million rising to STG 175 million in 2003. In Feb. 1999 ABN Amro predicted sales of STG 52 million in 2001 rising to STG 254 million in 2005.

AN 1999:339256 CAPLUS  
DN 131:138792  
TI SB-207499 SmithKline Beecham plc  
AU Brown, William M.  
CS Department of Anatomy & Physiology, University of Tasmania, Hobart, Australia  
SO Current Opinion in Anti-Inflammatory and Immunomodulatory Investigational Drugs (1999), 1(1), 39-47  
CODEN: COAIFF; ISSN: 1464-8474  
PB Current Drugs Ltd.  
DT Journal; General Review  
LA English

RE.CNT 108 THERE ARE 108 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN  
TI SB-207499. antiasthmatic/antiinflammatory, phosphodiesterase IV inhibitor  
AB A brief review with 49 refs. is given on cis-4-cyano-4-[3-(cyclopentyloxy)-4-methoxyphenyl]cyclohexane-1-carboxylic acid, SB-207499, ariflo, selected for treating allergic and inflammatory diseases. The 2nd-generation phosphodiesterase (PDE) 4 inhibitor SB-207499 under development is compared with corresponding drugs like rolipram, atizoram, piclamilast, V-11294A, and T-440. The PDE 4 inhibitory activities, the high-affinity rolipram binding site, the in vitro inhibitory activities on tumor necrosis factor- $\alpha$  production, on bronchoconstriction, and on cloned human PDE 4 subtypes are compared. Pharmacol. actions, pharmacokinetics, pharmacodynamics, and clin. studies are described. SB-207499 is currently in phase II testing in adults and pediatric patients with asthma and in phase III trials in patients with chronic obstructive pulmonary disease.

AN 1998:616407 CAPLUS

DN 130:79

TI SB-207499. antiasthmatic/antiinflammatory, phosphodiesterase IV inhibitor

AU Silvestre, J.; Graul, A.; Castaner, J.

CS Prous Science, Barcelona, 08080, Spain

SO Drugs of the Future (1998), 23(6), 607-615

CODEN: DRFUD4; ISSN: 0377-8282

PB Prous Science

DT Journal; General Review

LA English

RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 14:59:11 ON 22 AUG 2006)

FILE 'REGISTRY' ENTERED AT 14:59:37 ON 22 AUG 2006

EXP TIOTROPIUM/CN

L1 10 S E3-E12

EXP OXATROPIUM/CN

EXP OXITROPIUM/CN

L2 2 S E3-E4

EXP IPRATROPIUM/CN

L3 2 S E3-E4

0 S CLIOMILAST/CN

EXP ARIFLO/CN

L5 1 S ARIFLO/CN

L6 1 S ENPROFYLLINE/CN

L7 1 S ROFLUMILAST/CN

L8 STRUCTURE uploaded

L9 0 S L8

L10 23 S L8 SSS FULL

FILE 'CAPLUS' ENTERED AT 15:04:11 ON 22 AUG 2006

L11 881 S L1 OR L2 OR L3

L12 556 S L5 OR L6 OR L7 OR L10

L13 26 S L11 AND L12

L14 10 S L13 AND (ASTHSMA OR COPD OR (CHRONIC(W)OBSTRUCTIVE(W)PULMONAR

L15 0 S L14 NOT PY>2001

L16 0 S L14 NOT PY>2002

L17 237 S L11 AND (ASTHSMA OR COPD OR (CHRONIC(W)OBSTRUCTIVE(W)PULMONAR

L18 51 S L17 NOT PY>2001

L19 11 S L18 AND TIOTROPIUM

L20 0 S L19 AND ASTHSMA

L21 3 S L19 AND ASTHMA

L22 0 S L12 AND ASTHSMA AND (COPD OR (CHRONIC(W)OBSTRUCTIVE(W)PULMONAR

L23 85 S L12 AND (COPD OR (CHRONIC(W)OBSTRUCTIVE(W)PULMONARY(W)DISEASE

L24 14 S L23 NOT PY>2001

=> logoff

ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF

LOGOFF? (Y)/N/HOLD:Y

COST IN U.S. DOLLARS

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FULL ESTIMATED COST

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

	SINCE FILE ENTRY	TOTAL SESSION
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NEWS 11 JUN 26 TULSA/TULSA2 reloaded and enhanced with new search and  
and display fields  
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NEWS 13 JUL 11 CHEMSAFE reloaded and enhanced  
NEWS 14 JUL 14 FSTA enhanced with Japanese patents  
NEWS 15 JUL 19 Coverage of Research Disclosure reinstated in DWPI  
NEWS 16 AUG 09 INSPEC enhanced with 1898-1968 archive

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AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

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=> index bioscience patents

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FILE 'ENCOMPAT2' ACCESS NOT AUTHORIZED

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COST IN U.S. DOLLARS

SINCE FILE

**TOTAL**

FULL ESTIMATED COST

ENTRY	SESSION
0.21	0.21

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92 FILES IN THE FILE LIST IN STNINDEX

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=> s (anticholinergic or antimuscarinic) and (PDE4)

1 FILE BIOSIS  
6 FILE CAPLUS  
1 FILE DRUGU

33 FILES SEARCHED...

52 FILE IFIPAT  
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2 FILE PROMT  
6 FILE PROUSDDR  
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1 FILE TOXCENTER  
201 FILE USPATFULL  
27 FILE USPAT2  
32 FILE WPIDS  
6 FILE WPIFV  
32 FILE WPINDEX

69 FILES SEARCHED...

1 FILE DPCI  
36 FILE EPFULL  
16 FILE INPADOC  
305 FILE PCTFULL

19 FILES HAVE ONE OR MORE ANSWERS, 92 FILES SEARCHED IN STNINDEX

L1 QUE (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4)

=> file uspatfull epfull pctfull

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
1.83	2.04

FULL ESTIMATED COST

FILE 'USPATFULL' ENTERED AT 16:26:03 ON 22 AUG 2006

CA INDEXING COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EPFULL' ENTERED AT 16:26:03 ON 22 AUG 2006

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FILE 'PCTFULL' ENTERED AT 16:26:03 ON 22 AUG 2006

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=> s (anticholinergic or antimuscarinic) and (PDE4)

L2 542 (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4)

=> s (anticholinergic or antimuscarinic) and (PDE4(w) inhibit?)

L3 514 (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4(W) INHIBIT?)

=> s l3 not py>2001

L4 6 L3 NOT PY>2001

=> d 14 1-6 ti

L4 ANSWER 1 OF 6 USPATFULL on STN  
TI Anti-allergy anti-inflammatory composition

L4 ANSWER 2 OF 6 EPFULL COPYRIGHT 2006 EPO/FIZ KA on STN  
TIEN Prokinetic agents for treating gastric hypomotility and related disorders.  
TIFR Agents prokinetiques pour le traitement de l'hypomobilite gastrique et des troubles similaires.  
TIDE Prokinetische Arzneimittel zur Behandlung von Magen Hypomobilitaets- und vergleichbaren Erkrankungen.

L4 ANSWER 3 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN  
TIEN THE TREATMENT OF RESPIRATORY DISEASES  
TIFR TRAITEMENT DE TROUBLES RESPIRATOIRES

L4 ANSWER 4 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN  
TIEN NICOTINAMIDE BENZOFUSED-HETEROCYCLYL DERIVATIVES USEFUL AS SELECTIVE INHIBITORS OF PDE4 ISOZYMES  
TIFR DERIVES BENZOCONDENSES HETEROCYCLIQUES DE NICOTINAMIDE UTILES COMME INHIBITEURS SELECTIFS D'ISOZYMES PDE4

L4 ANSWER 5 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN  
TIEN PYRIMIDINE CARBOXAMIDES USEFUL AS INHIBITORS OF PDE4 ISOZYMES  
TIFR CARBOXAMIDES DE PYRIMIDINE UTILISES COMME INHIBITEURS DES ISOZYMES PDE4

L4 ANSWER 6 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN  
TIEN INDAZOLE BIOISOSTERE REPLACEMENT OF CATECHOL IN THERAPEUTICALLY ACTIVE COMPOUNDS  
TIFR REMPLACEMENT BIOISOSTHERE DU CATECHOL PAR L'INDAZOLE DANS DES COMPOSES THERAPEUTIQUEMENT ACTIFS

=> d 14 1-6 ti abs bib

L4 ANSWER 1 OF 6 USPATFULL on STN  
TI Anti-allergy anti-inflammatory composition  
AB A novel composition of Nimesulide and salts thereof and Cetirizine possessing antileukotriene, antihistaminic, antiallergic and antiinflammatory action is disclosed. The composition is useful in the cure of allergic disorders such as rhinitis, bronchitis, asthma, urticaria and the like.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AN 2001:107898 USPATFULL  
TI Anti-allergy anti-inflammatory composition  
IN Singh, Amarjit, New Delhi, India  
Jain, Rajesh, New Delhi, India  
PA Panacea Biotec Limited, New Delhi, India (non-U.S. corporation)  
PI US 6258816 B1 20010710  
AI US 1998-178652 19981026 (9)  
PRAI IN 1997-318597 19971106  
DT Utility  
FS GRANTED  
EXNAM Primary Examiner: Geist, Gary; Assistant Examiner: White, Everett  
LREP Oblon, Spivak, McClelland, Maier & Neustadt, P.C.  
CLMN Number of Claims: 11  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 681  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 2 OF 6 EPFULL COPYRIGHT 2006 EPO/FIZ KA on STN  
TIEN Prokinetic agents for treating gastric hypomotility and related disorders.  
TIFR Agents prokinetiques pour le traitement de l'hypomobilite gastrique et

des troubles similaires.

TIDE Prokinetische Arzneimittel zur Behandlung von Magen Hypomobilitaets- und vergleichbaren Erkrankungen.

ABEN

The invention describes the use of PDE-4 (phosphodiesterase-4) inhibitors in the treatment or prevention of gastric stasis resulting from hypomotility of the stomach (with delayed emptying of the liquid and/or solid contents of the stomach).

More particularly said inhibitors are indazole derivatives such as (1H-indazol-6-yl)-cyclohexane or cyclohexene carboxylic acid derivatives, carbonitriles, amides or esters thereof. Gastric or gastrointestinal disorders, which may also be caused by adverse effects of therapeutic agents, of surgical operations or concomitant or secondary aspects of another disease, which include pain, nausea, vomiting, heartburn, postprandial discomfort, indigestion and gastro-esophageal reflux, can be prevented or treated with pharmaceutical compositions containing said PDE-4 indazole inhibitors.

AN 1999:109036 EPFULL  
DUPD 20001018 DUPW 200042  
TIEN Prokinetic agents for treating gastric hypomotility and related disorders.  
TIFR Agents prokinetiques pour le traitement de l'hypomobilité gastrique et des troubles similaires.  
TIDE Prokinetische Arzneimittel zur Behandlung von Magen Hypomobilitaets- und vergleichbaren Erkrankungen.  
IN Watson, John Wesley, 13 Cranwood Road, Ledyard, Connecticut 06339, US;  
Woods, Anthony John, Wellcome Trust, 183 Euston Road, London NW1 2BN,  
GB;  
Andrews, Paul, St. Georges Hospital Med. School, Department Physiology,  
Cranmer Terrace, Tooting, London SW17 0RE, GB  
PA PFIZER INC., 235 East 42nd Street, New York, N.Y. 10017, US  
PAN 200961  
AG Simpson, Alison Elizabeth Fraser, et al, Urquhart-Dykes & Lord, 30  
Welbeck Street, London W1M 7PG, GB  
AGN 77401  
DT Patent  
LAF English  
LA English  
LAP English  
TL German; English; French  
PIT EPA3 Separate publication of search report  
PI EP 1040829 A3 20001018  
DS AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE  
EXTENSION STATES: AL LT LV MK RO SI  
AI EP 1999-310202 A 19991216  
PRAI US 1998-114217P P 19981230  
  
L4 ANSWER 3 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN  
TIEN THE TREATMENT OF RESPIRATORY DISEASES  
TIFR TRAITEMENT DE TROUBLES RESPIRATOIRES  
ABEN A pharmaceutical composition for pulmonary delivery comprises glycopyrrolate in a controlled release formulation, wherein, on administration, the glycopyrrolate exerts its pharmacological effect over a period greater than 12 hours.  
ABFR La presente invention concerne une composition pharmaceutique destinee a une administration pulmonaire, comprenant du glycopyrrolate dans une formulation a libération controlee. Lorsque ladite composition a ete administree, le glycopyrrolate exerce son action pharmacologique pendant une periode superieure a 12 heures.  
AN 2001076575 PCTFULL ED 20020822  
TIEN THE TREATMENT OF RESPIRATORY DISEASES  
TIFR TRAITEMENT DE TROUBLES RESPIRATOIRES

IN BANNISTER, Robin, Mark;  
 RICHARDS, Andrew, John, McGlashan;  
 GILBERT, Julian, Clive;  
 MORTON, David, A., V.;  
 STANIFORTH, John

PA ARAKIS LTD.;  
 BANNISTER, Robin, Mark;  
 RICHARDS, Andrew, John, McGlashan;  
 GILBERT, Julian, Clive;  
 MORTON, David, A., V.;  
 STANIFORTH, John

DT Patent

PI WO 2001076575 A2 20011018

DS W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU  
 CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS  
 JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW  
 MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ  
 UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG  
 ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR  
 GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GW  
 ML MR NE SN TD TG

AI WO 2001-GB1606 A 20010409

PRAI GB 2000-0008660.3 20000407

L4 ANSWER 4 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN

TIEN NICOTINAMIDE BENZOFUSED-HETEROCYCLYL DERIVATIVES USEFUL AS SELECTIVE INHIBITORS OF PDE4 ISOZYMES

TIFR DERIVES BENZOCONDENSES HETEROCYCLIQUES DE NICOTINAMIDE UTILES COMME INHIBITEURS SELECTIFS D'ISOZYMES PDE4

ABEN Compounds useful as inhibitors of PDE4 in the treatment of diseases regulated by the activation and degranulation of eosinophils, especially asthma, chronic bronchitis, and chronic obstructive pulmonary disease, of Formula (1.0.0.). In said formula R5 and R6 are taken together to form a moiety of partial Formulas (1.1.1) through (1.1.5) or a pharmaceutically acceptable salt thereof.

ABFR L'invention a trait a des composes utiles comme inhibiteurs de PDE4 dans le traitement de maladies regulees par l'activation et la degranulation de polynucleaires eosinophiles, specialement l'asthme, la bronchite chronique et la bronchopneumopathie obstructive chronique ; ou a un sel pharmaceutiquement acceptable de ces composes. Les composes sont representes par la formule (1.0.0), dans laquelle R5 et R6 forment ensemble une fraction des formules partielles (1.1.1) a (1.1.5).

AN 2001057036 PCTFULL ED 20020827

TIEN NICOTINAMIDE BENZOFUSED-HETEROCYCLYL DERIVATIVES USEFUL AS SELECTIVE INHIBITORS OF PDE4 ISOZYMES

TIFR DERIVES BENZOCONDENSES HETEROCYCLIQUES DE NICOTINAMIDE UTILES COMME INHIBITEURS SELECTIFS D'ISOZYMES PDE4

IN MARFAT, Anthony;  
 CHAMBER, Robert, James

PA PFIZER PRODUCTS INC.;  
 MARFAT, Anthony;  
 CHAMBER, Robert, James

DT Patent

PI WO 2001057036 A1 20010809

DS W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ  
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 GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GW ML  
 MR NE SN TD TG

AI WO 2001-IB124 A 20010130

PRAI US 2000-60/179,284 20000131

L4 ANSWER 5 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN  
TIEN PYRIMIDINE CARBOXAMIDES USEFUL AS INHIBITORS OF PDE4 ISOZYMES  
TIFR CARBOXAMIDES DE PYRIMIDINE UTILISES COMME INHIBITEURS DES ISOZYMES PDE4  
ABEN Compounds of formula (1.0.0) are described, as well as the usefulness of  
a pharmaceutical composition for treating inflammatory, respiratory and  
allergic diseases and conditions, especially asthma; chronic obstructive  
pulmonary disease (COPD) including chronic bronchitis, emphysema, and  
bronchiectasis; chronic rhinitis; and chronic sinusitis.

ABFR L'invention concerne des composes correspondant a la formule (1.0.0)  
ainsi que l'utilisation d'une composition pharmaceutique dans le  
traitement des maladies et etats inflammatoires, respiratoires et  
allergiques et notamment de l'asthme; de la BPCO (broncho-pneumopathie  
chronique obstructive), y compris la bronchite chronique, l'emphyseme et  
la bronchectasie, la rhinite chronique et la sinusite chronique.

AN 2001057025 PCTFULL ED 20020827  
TIEN PYRIMIDINE CARBOXAMIDES USEFUL AS INHIBITORS OF PDE4 ISOZYMES  
TIFR CARBOXAMIDES DE PYRIMIDINE UTILISES COMME INHIBITEURS DES ISOZYMES PDE4  
IN CHAMBERS, Robert, James;  
MAGEE, Thomas, Victor;  
MARFAT, Anthony  
PA PFIZER PRODUCTS INC.;  
CHAMBERS, Robert, James;  
MAGEE, Thomas, Victor;  
MARFAT, Anthony  
DT Patent  
PI WO 2001057025 A1 20010809  
DS W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ  
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MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA  
UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZW  
AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB  
GR IE IT LU MC NL PT SE TR BF BJ CF CG CI CM GA GN GW ML  
MR NE SN TD TG

AI WO 2001-IB125 A 20010130  
PRAI US 2000-60/179,282 20000131

L4 ANSWER 6 OF 6 PCTFULL COPYRIGHT 2006 Univentio on STN  
TIEN INDAZOLE BIOISOSTERE REPLACEMENT OF CATECHOL IN THERAPEUTICALLY ACTIVE  
COMPOUNDS  
TIFR REMPLACEMENT BIOISOSTHERE DU CATECHOL PAR L'INDAZOLE DANS DES COMPOSES  
THERAPEUTIQUEMENT ACTIFS  
ABEN Therapeutically active compositions of matter and member species thereof  
are described which  
comprise indazole-containing compounds, said compounds and their  
therapeutic activity resulting  
directly from an indazole-for-catechol bioisostere replacement of a  
catechol-containing compound  
having the same therapeutic activity, where non-catechol substituents  
are the same or homologous  
before and after said replacement, and wherein said compositions of  
matter comprise a compound of  
Formula (I1&quest;) or (I2&quest;), or a pharmaceutically acceptable  
salt thereof, wherein in a preferred  
embodiment RC&quest; is hydrogen; RA&quest; is cyclohexyl; and  
RB&quest; is ethyl. R&quest;a and R&quest;b are each individually  
and independently hydrogen or non-catechol substituents of said  
compounds resulting directly from an  
indazole-for-catechol bioisotere replacement of said catechol-containing  
compound having said  
therapeutic activity, where said non-catechol substituents are the same  
or homologous before and  
after said replacement, provided that both of R&quest;a and R&quest;b  
cannot be hydrogen at the same time. The  
therapeutic activity involved may comprise cholinesterase inhibitory

activity, adrenergic  
&alpha;&quest;1-antagonist and &beta;&quest;1-agonist activity,  
calcium channel inhibitory activity,  
antineoplastic activity, and phosphodiesterase type IV inhibitor  
activity.

ABFR La presente invention concerne, d'une part des compositions  
therapeutiquement actives a base de  
substances et d'espèces appartenant a ces substances, lesquelles  
compositions comprennent des  
composes contenant de l'indazole, ou d'autre part certains des sels  
derives pharmaceutiquement  
admis. En l'occurrence, les composes consideres, et leur activite  
therapeutique, resultent  
directement d'un remplacement bioisosthere du catechol par l'indazole  
dans des composes contenant du  
catechol et presentant la même activite therapeutique, les substituants  
non-catechol etant les memes  
ou homologues avant et apres ledit remplacement. Les compositions a base  
de la substance consideree  
comprènnent un compose represente par la formule generale (I?1&quest;)  
ou (I?2&quest;). Dans une realisation  
preferee, R?C&quest; est hydrogene, R?A&quest; est cyclohexyle, et  
R?B&quest; est ethyle. R&quest;a? et R&quest;b? sont chacun  
individuellement et independamment hydrogene ou substituant non catechol  
des composes consideres  
resultant directement d'un remplacement bioisosthere du catechol par  
l'indazole dans le compose  
considere contenant du catechol et presentant une activite  
therapeutique. En l'occurrence, lesdits  
substituants non catechol sont les memes ou homologue avant et apres le  
remplacement considere, sous  
la reserve que R&quest;a? et R&quest;b? ne soient pas en meme temps  
hydrogene. L'activite therapeutique  
consideree peut etre une activite inhibitrice de la cholinesterase, une  
activite adrenergique  
&alpha;&quest;1-antagoniste et &beta;&quest;1-agoniste, une activite  
inhibitrice du canal calcium, une  
activite antineoplasique, voire une activite inhibitrice des  
phosphodiesterases de type IV.

AN 1999023077 PCTFULL ED 20020515

TIEN INDAZOLE BIOISOSTERE REPLACEMENT OF CATECHOL IN THERAPEUTICALLY ACTIVE  
COMPOUNDS

TIFR REMPLACEMENT BIOISOSTHERE DU CATECHOL PAR L'INDAZOLE DANS DES COMPOSES  
THERAPEUTIQUEMENT ACTIFS

IN MARFAT, Anthony

PA PFIZER PRODUCTS INC.;

MARFAT, Anthony

LA English

DT Patent

PI WO 9923077 A1 19990514

DS W:  
AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES  
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LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE  
SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH GM KE LS  
MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE  
DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM  
GA GN GW ML MR NE SN TD TG

AI WO 1998-IB1710 A 19981026

PRAI US 1997-60/064,229 19971104

US 1997-60/064,187 19971104

US 1997-60/064,024 19971104

US 1997-60/064,228 19971104

US 1997-60/064,198 19971104

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(FILE 'HOME' ENTERED AT 16:24:23 ON 22 AUG 2006)

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE, AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS, CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 16:24:33 ON 22 AUG 2006  
SEA (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4)

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1 FILE BIOSIS  
6 FILE CAPLUS  
1 FILE DRUGU  
52 FILE IFIPAT  
2 FILE PHIN  
2 FILE PROMT  
6 FILE PROUSDDR  
1 FILE RDISCLOSURE  
1 FILE SCISEARCH  
1 FILE TOXCENTER  
201 FILE USPATFULL  
27 FILE USPAT2  
32 FILE WPIDS  
6 FILE WPIFV  
32 FILE WPINDEX  
1 FILE DPCI  
36 FILE EPFULL  
16 FILE INPADOC  
305 FILE PCTFULL

L1 QUE (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4)

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L2 542 S (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4)  
L3 514 S (ANTICHOLINERGIC OR ANTIMUSCARINIC) AND (PDE4 (W) INHIBIT?)  
L4 6 S L3 NOT PY>2001

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ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF

LOGOFF? (Y)/N/HOLD:Y

COST IN U.S. DOLLARS

FULL ESTIMATED COST

SINCE FILE ENTRY	TOTAL SESSION
13.46	15.50

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